

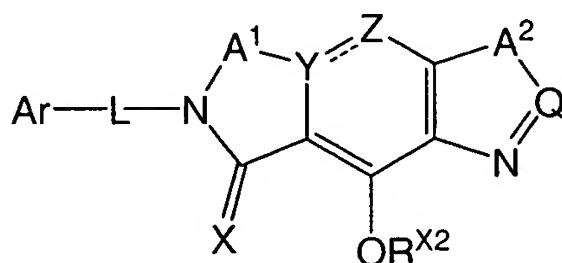


Amendment to the Specification

SUMMARY OF THE INVENTION

The present invention provides compositions and methods for inhibition of HIV integrase.

In one aspect, the invention ~~comprises~~ is a compound having the structure:

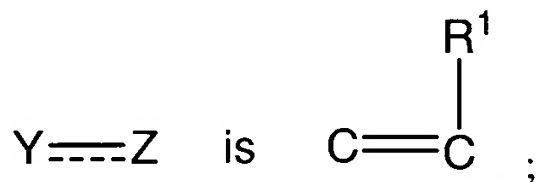


wherein:

A¹ is independently selected from C(R²)₂, CR²OR, CR²OC(=O)R, C(=O), C(=S), CR²SR, and C(=NR),

A² is independently selected from C(R²)₂-C(R³)₂, C(R²)=C(R³), and C(=O)C(R³)₂;

Q is CR⁴;



L is selected from a bond, O, S, S-S, S(=O), S(=O)₂, S(=O)₂NR, NR, N-OR, C₁-C₁₂ alkylene, C₁-C₁₂ substituted alkylene, C₂-C₁₂ alkenylene, C₂-C₁₂ substituted alkenylene, C₂-C₁₂ alkynylene, C₂-C₁₂ substituted alkynylene, C(=O)NH, OC(=O)NH, NHC(=O)NH, C(=O), C(=O)NH(CH₂)_n, or (CH₂CH₂O)_n, where n is optionally 1, 2, 3, 4, 5, or 6;

X is selected from O, S, NH, NR, N-OR, N-NR₂, N-CR₂OR and N-CR₂NR₂;

Ar is selected from (a) a C₃-C₁₂ carbocycle, C₃-C₁₂ substituted carbocycle, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl;

or (b) a saturated, unsaturated or aromatic ring or ring system having a mono- or bicyclic carbocycle or heterocycle containing 3 to 12 ring atoms;

R², R³ and R⁴ are each independently selected from H, F, Cl, Br, I, OH, -NH₂, -NH₃⁺, -NHR, -NR₂, -NR₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈

alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R, -SO₂Ar, -SOAr, -SAr, -SO₂NR₂, -SOR, -CO₂R, -C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₃-C₁₂ carbocycle, C₃-C₁₂ substituted carbocycle, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

when taken together on a single carbon, two R² or two R³ may form a spiro ring; R¹ is independently selected from CR₃, NRSO₂R, OC(=O)NR₂, OC(=O)R, SR, H, F, Cl, Br, I, OH, -NH₂, -NH₃⁺, -NHR, -NR₂, -NR₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈ alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R, -SO₂Ar, -SOAr, -SAr, -SO₂NR₂, -SOR, -CO₂R, -C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₃-C₁₂ carbocycle, C₃-C₁₂ substituted carbocycle, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

R is independently selected from H, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

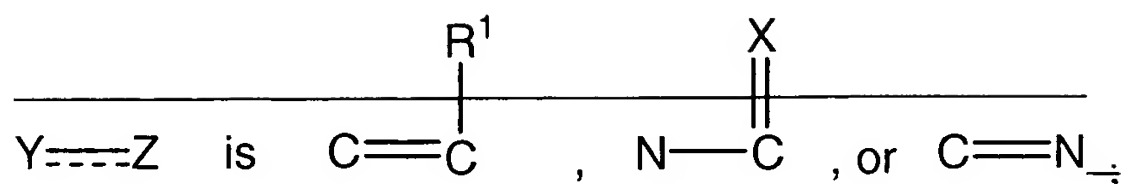
R^{X2} is independently selected from H, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₂-C₂₀ heteroaryl, and C₂-C₂₀ substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, a prodrug moiety, and a protecting group;

and the tautomers, salts, solvates, resolved enantiomers and purified diastereomers thereof;

with the proviso that when Y=Z is C=C(OH), X is O, A¹ is C(=O), A² is C(R²)=C(R³), and Q is CH, then L is not a bond.

A¹ and A² are independently selected from O, S, NR, C(R²)₂, CR²OR, CR²OC(=O)R, C(=O), C(=S), CR²SR, C(=NR), C(R²)₂-C(R³)₂, C(R²)=C(R³), C(R²)₂-O, NR-C(R³)₂, N=C(R³), N=N, SO₂-NR, C(=O)C(R³)₂, C(=O)NR, C(R²)₂-C(R³)₂-C(R³)₂, C(R²)=C(R³)-C(R³)₂, C(R²)C(=O)NR, C(R²)C(=S)NR, C(R²)=N-C(R³)₂, C(R²)=N-NR, and N=C(R³)-NR;

Q is N, ⁺NR, or CR⁴;



~~L is selected from a bond, O, S, S-S, S(=O), S(=O)₂, S(=O)₂NR, NR, N-OR, C₁-C₁₂ alkylene, C₁-C₁₂-substituted alkylene, C₂-C₁₂-alkenylene, C₂-C₁₂-substituted alkenylene, C₂-C₁₂ alkynylene, C₂-C₁₂-substituted alkynylene, C(=O)NH, OC(=O)NH, NHC(=O)NH, C(=O), C(=O)NH(CH₂)_n, or (CH₂CH₂O)_n, where n may be 1, 2, 3, 4, 5, or 6;~~

~~X is selected from O, S, NH, NR, N-OR, N-NR₂, N-CR₂OR and N-CR₂NR₂;~~

~~Ar is selected from C₃-C₁₂-carbocycle, C₃-C₁₂-substituted carbocycle, C₆-C₂₀-aryl, C₆-C₂₀-substituted aryl, C₂-C₂₀-heteroaryl, and C₂-C₂₀-substituted heteroaryl;~~

~~R¹, R², R³ and R⁴ are each independently selected from H, F, Cl, Br, I, OH, -NH₂, -NH₃⁺, -NHR, -NR₂, -NR₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈ alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R, -SO₂Ar, -SOAr, -SAr, -SO₂NR₂, -SOR, -CO₂R, -C(=O)NR₂, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₁-C₈-substituted alkyl, C₃-C₁₂-carbocycle, C₃-C₁₂-substituted carbocycle, C₆-C₂₀-aryl, C₆-C₂₀-substituted aryl, C₂-C₂₀-heteroaryl, and C₂-C₂₀-substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;~~

~~when taken together on a single carbon, two R² or two R³ may form a spiro ring; and~~

~~R is independently selected from H, C₁-C₈ alkyl, C₁-C₈-substituted alkyl, C₆-C₂₀-aryl, C₆-C₂₀-substituted aryl, C₂-C₂₀-heteroaryl, and C₂-C₂₀-substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;~~

~~R^{X2} is independently selected from H, C₁-C₈ alkyl, C₁-C₈-substituted alkyl, C₆-C₂₀-aryl, C₆-C₂₀-substituted aryl, C₂-C₂₀-heteroaryl, and C₂-C₂₀-substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, a prodrug, a pharmaceutically acceptable prodrug, a prodrug moiety, a protecting group, and a phosphonate prodrug moiety;~~

~~and the salts, solvates, resolved enantiomers and purified diastereomers thereof;~~

~~with the proviso that when Y=Z is C=C(OH), X is O, A¹ is C(=O), A² is C(R²)=C(R³), and Q is CH, then L is not a bond.~~